

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
28 November 2002 (28.11.2002)

PCT

(10) International Publication Number
WO 02/094297 A1

(51) International Patent Classification⁷: **A61K 35/78**,
33/22, A61P 25/36, 25/20, 43/00

(21) International Application Number: PCT/AU02/00649

(22) International Filing Date: 23 May 2002 (23.05.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PR 5207 23 May 2001 (23.05.2001) AU

(71) Applicant and

(72) Inventor: **LIU, Xiaoming** [AU/AU]; 24 Patrick Street,
Hurstville, New South Wales 2220 (AU).

(74) Agents: **HALFORD, Graham, William** et al.; Halford &
Co., Level 7, 1 Market Street, Sydney, New South Wales
2000 (AU).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG,
SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent
(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG).

Published:

— with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: HERBAL COMPOSITION FOR THE TREATMENT OF DRUG ADDICTION AND INSOMNIA

(57) Abstract: The present invention relates to compositions including Borax and the herbs *Radix Ginseng* and *Radix Gentianae*, or extracts thereof, which are useful in treating drug addiction, particularly opiate addiction. The compositions may include other herbs or their extracts, and may be useful for treating of insomnia.



WO 02/094297 A1

HERBAL COMPOSITION FOR THE TREATMENT OF DRUG ADDICTION AND INSOMNIA

TECHNICAL FIELD

5 This invention relates to compositions derived using traditional Chinese medicine practices and to the use of such compositions in the treatment of human diseases and disorders.

In particular the invention relates to a treatment of drug addiction and insomnia by administering to a patient a novel combination of Chinese herbs and extracts.
10

BACKGROUND ART

Drug addiction, in particular opiate addiction, and insomnia are major health problems and the successful treatment of these conditions poses a great challenge to the medical
15 profession.

It is known that drug addiction can be blocked, and withdrawal or detoxification effected, by treatment with opiate agonist such as Methadone.

20 However, methadone is itself addictive and its use in withdrawal is restricted to treatment periods of not more than a few weeks to carry the addict through the acute withdrawal stage. Methadone is not a good agent for maintaining abstinence from the drug after withdrawal is achieved. As a result, the relapse rate after Methadone – based treatment is high.

25 The present invention is based on the discovery that some compositions of Chinese herbs have a powerful effect in blocking drug addiction and treatment of insomnia. It is an object of the present invention to provide an effective non-opiate based treatment which avoids one or more of the disadvantages of current treatment.

SUMMARY OF THE INVENTION

According to a first aspect, the invention resides in a composition including borax,
5 ginseng and gentian root, or extracts thereof.

In a preferred embodiment the invention resides in a composition which further includes chicken's gallbladder or extract thereof.

10 According to a second aspect, the invention resides in a composition including borax, ginseng and gentian root, Chinese lobelia and/or notoginseng, or extracts thereof.

In another preferred embodiment, the invention resides in a composition which further includes one or more of oyster shell, white peony, rhubarb, ginger, unsalted fermented
15 soybean, gardenia flower, scutellari root, unripe bitter orange, houttunzia, bupleurum root, licorice, gizzard lining, spiny jujube kernel, peanut leaf and manyprickle acanthopanax root, or extracts thereof.

According to a third aspect, the invention resides in a medicament for the treatment of
20 drug addiction and insomnia including an effective amount of any one of the compositions described above.

In a fourth aspect, the invention resides in a method for treating drug addiction and insomnia in a patient including administering to said patient an effective amount of
25 any one of the compositions described above.

According to a fifth aspect, the invention resides in a method for preparing any one of the compositions described above.

DESCRIPTION OF PREFERRED EMBODIMENTS

A composition according to the invention can be manufactured from the following
5 components (English/Latin):

1. Borax (Borax) 0.5-8 parts, preferably 1-4 parts
2. Ginseng (Radix Ginseng) 0.5-4 parts, preferably 0.8-2.1 parts
3. Gentian root (Radix Gentianae) 0.5-8 parts, preferably 1-4 parts
- 10 4. Chicken's gallbladder 0.5-4 parts, preferably 0.8-2.1 parts
5. Chinese Lobelia (Lobeliae Chinensis Herba Cum Radice) 0.5-10 parts, preferably 2-6 parts
6. Notoginseng root (Notoginseng Radix) 0-4 parts, preferably 1-2.1 parts
7. Oyster shell (Concha Ostreae) 0-9 parts, preferably 2-5 parts
- 15 8. White peony (Radix Paeoniae Albae) 0 - 11 parts, preferably 2.2-6.2 parts
9. Rhubarb (Rhizoma Rhei) 0-9 parts, preferably 2-5 parts
10. Fresh ginger (Zingiberis Rhizoma Recens) 0-11 parts, preferably 2.1-6.2 parts
11. Fermented soybean unsalted (Glycines Semen Fermentatum Insulsum) 0-9 parts, preferably 2-5 parts
- 20 12. Gardenia flower (Gardeniae Flos) 0-9 parts, preferably 2-5 parts
13. Scutellari root (Scutellariae Radix) 0-4.5 parts, preferably 1-2.2 parts
14. Unripe bitter orange (Aurantii Fructus Immaturus) 0.4-5 parts, preferably 1.2-2 parts
15. Houttuynia (Houttuyniae Herba Cum Radice) 0-11 parts, preferably 2.2-6.2 parts
- 25 16. Bupleurum root (Radix Bupleuri) 0-4 parts, preferably 1-2 parts
17. Chicken Gizzard Lining (Endothelium Corneum Gigeriae Galli) 0-10 parts, preferably 2.2-5.2 parts
18. Licorice (Radix Glycyrrhizae) 0 - 11 parts, preferably 2.2 - 6.2 parts
19. Spiny jujube kernel (Semen Ziziphi Spinosae) 6-16 parts, preferably 8-14 parts
- 30 20. Peanut leaf 6-16 parts, preferably 8-14 parts
21. Manyprickle Acanthopanax root (Radix Acanthopanax senticosi) 2-10 parts, preferably 4-7 parts

The relative ratios of components represent dry weights of components prior to the extraction processes described below.

- 5 In preparing the composition, the appropriate amounts of cut herbal pieces were first soaked together in water at a temperature of 30-60°C for 2-4 hours.

Extract of borax and oyster shell was produced by placing in alcohol at a temperature of 60-70°C for 24-48 hours, a cycle that was repeated three times. The alcohol must
10 cover the oyster shells and borax.

Extract of ginseng and notoginseng root was produced by decoction in water for 40 minutes repeated three times.

- 15 The extract of rhubarb was prepared by decocting the cut rhubarb pieces in water for a session of 15 minutes followed by two sessions of 20 minutes.

The remaining herbs were prepared together by decocting three times in water for 30 minutes.

20 In the above-described decoction processes, water must cover the top of cut herbal pieces by about 1 cm.

The extracted liquids were then combined, distilled and evaporated to produce a dry
25 powder to which was added a chicken gizzard membrane powder.

Although the administration of a composition not containing Chicken's gallbladder will be effective in treating drug addiction and insomnia, it is discovered that is desirable to add liquid extract pressed from the chicken's gallbladder that has been
30 disinfected in ethanol.

The resultant paste was placed in capsules ready for ingestion, each capsule containing 0.5g of the composition.

Alternatively, Gizzard lining may be soaked and decocted together with other herbal pieces. Also, a liquid extract pressed from the chicken's gallbladder may be added to the liquids extracted from the herbal pieces, borax, gizzard lining, and oyster shells. The obtained mixture is then distilled and evaporated to produce a dry powder. The dry powder may be placed in capsules, each capsule containing 0.5 g of the powder.

The dosage may be varied according to the condition treated and the concentration of active ingredients used. Thus, consumption of 4-5 capsules orally every eight hours is recommended for treatment of drug addiction. The dosage for treatment of insomnia is 2 capsules orally 4 hours prior to a normal sleeping period, followed by 2 capsules orally 0.5 hour prior to said normal sleeping period.

15

EXAMPLE

A clinical trial was conducted involving 398 heroin addicts with an average 7.9 year addiction and a varying degree of usage.

202 patients were chosen at random to be administered with the composition of the invention, 196 patients were administered with methadone as a control group.

In each group, opiate intake was abruptly stopped and treatment commenced after 10 hours. Patients receiving the new treatment received 6-8 capsules, modified according to body weight and heroin usage, orally every four hours for up to 10 days.

25

Patients receiving methadone were administered a dose according to body weight and heroin use, the dose being decreased at a rate of 25% per day to zero over 10 days.

The patients were assessed and scored by trained nurses according to the severity of classic withdrawal symptoms exhibited by the patient. The symptoms assessed were nausea, stomach cramps, muscle spasms, feelings of coldness, heart pounding,

30

muscular tension, aches and pains, yawning, watery eyes, insomnia, lachrymation and perspiring.

5 The patients also underwent a self examination where they were asked to rate their own feelings of calmness, anger, cold turkey, drug craving, dry mouth, drowsiness and general well being.

In the assessments, neither the patient nor the clinician were aware whether the patient's treatment involved methadone or the inventive composition.

10

The results of the trial were that the new composition of the invention as a treatment of drug addiction compares favourably with methadone, a well known drug replacement therapy. However, the present invention has a further advantage in that it is a non-opiate based treatment and thus does not have the addictive side-effects that
15 methadone can sometimes have.

20

The studies to date show that the composition described can effectively treat drug addiction and withdrawal in 90% of cases within 7 days and the remaining 10% within 10 days.

Further studies have shown that if treatment with a composition according to the invention is continued for 3 to 6 months after drug withdrawal, the relapse rate can be significantly reduced.

25 While particular embodiments of this invention have been described, it will be evident to those skilled in the art that the present invention may be embodied in other specific forms without departing from the essential characteristics thereof. The present embodiments and examples are therefore to be considered in all respects as illustrative and not restrictive, and all modifications which would be obvious to those skilled in
30 the art are therefore intended to be embraced therein. It will further be understood that any reference herein to known prior art does not, unless the contrary indication

appears, constitute an admission that such prior art is commonly known by those skilled in the art to which the invention relates.

CLAIMS:

1. A composition including Borax, the herbs *Radix Ginseng* (ginseng) and *Radix Gentianae* (gentian root), or extracts thereof.
5
2. A composition according to claim 1 further including chicken's gallbladder, or extract thereof.
- 10 3. A composition according to claim 1 or 2 further including the herb *Lobeliae Chinensis Herba Cum Radice* (Chinese lobelia), or extract thereof.
4. A composition according to claim 1 or 2 further including the herb *Notoginseng Radix* (notoginseng root), or extract thereof.
15
5. A composition according to claim 1 or 2 further including the herbs *Lobeliae Chinensis Herba Cum Radice* (Chinese lobelia) and/or *Notoginseng Radix* (notoginseng root), or extracts thereof.
- 20 6. A composition according to any one of claims 1- 5 further including one or more of *Rhizoma Rhei* (rhubarb), *Radix Bupleuri* (bupleurum root), *Houttuyniae Herba Cum Radice* (houttunya) and *Aurantii Fructus Immaturus* (unripe bitter orange), or extracts thereof.
- 25 7. A composition according to claim 6 further including one or more of *Concha Ostreae* (oyster shell), *Radix Paeoniae Albae* (white peony), *Zingiberis Rhizoma Recens* (fresh ginger), *Glycines Semen Fermentatum Insulsum* (unsalted fermented soybean), *Gardeniae Flos* (gardenia flower), *Scutellariae Radix* (scutellari root) ,
Radix Glycyrrhizae (licorice), *Endothelium Corneum Gigeriae Galli* (gizzard lining) ,
30 *Semen Ziziphi Spinosae* (spiny jujube kernel), peanut leaf and *Radix Acanthopanaxis Senticosi* (manyprickle acanthopanax root), or extracts thereof.

8. A composition according to claim 7 including 1-4 parts Borax, 0.8-2.1 parts Ginseng (*Radix Ginseng*), 0.8-2.1 parts Chicken's gallbladder, 1-4 parts Gentian root (*Radix Gentianae*), 2-6 parts Chinese Lobelia (*Lobeliae Chinensis Herba Cum Radice*), 1-2.1 parts Notoginseng root (*Notoginseng Radix*), 2-5 parts Oyster shell (*Concha Ostreae*), 2.2-6.2 parts White peony (*Radix Paeoniae Albae*), 2-5 parts Rhubarb (*Rhizoma Rhei*), 2.1-6.2 parts Fresh ginger (*Zingiberis Rhizoma Recens*), 2-5 parts Fermented soybean unsalted (*Glycines Semen Fermentatum Insulsum*), 2-5 parts Gardenia flower (*Gardeniae Flos*), 1-2.2 parts Scutellari root (*Scutellariae Radix*), 1.2-2 parts Unripe bitter orange (*Aurantii Fructus Immaturus*), 2.2-6.2 parts Houltuynia (*Houltuyniae Herba Cum Radice*), 1-2 parts Bupleurum root (*Radix Bupleuri*), 2.2-5.2 parts Gizzard Lining (*Endothelium Corneum Gigeriae Galli*), 2.2-6.2 parts Licorice (*Glycyrrhizae Radix*), 8-14 parts Sping jujube kernel (*Semen Ziziphi Spinosae*); 8-14 parts Peanut leaf and 4-7 parts Manyprickle Acanthopanax root (*Radix Acanthopanaxis senticosi*), or extracts thereof.
9. A composition according to any one of claims 1 to 8, wherein the composition is in the form of a liquid.
10. A composition according to any one of claims 1 to 8, wherein the composition is in the form of a powder.
11. A composition according to any one of claims 1 to 8, wherein the composition is in the form of a paste.
12. A composition according to any one of claims 1 to 8, wherein the composition is in the form of a capsule.
13. A method of preparing a medicinal composition for treating drug addiction and insomnia including the steps of :
- soaking effective amounts of dry cut herbs selected from the following group:
ginseng, notoginseng, rhubarb, gentian root, Chinese lobelia, unripe bitter orange,

- white peony, ginger, unsalted fermented soybean, gardenia flower, scutellari root, houttunzia, bupleurum root, licorice, spiny jujube kernel, peanut leaf, and manyprickle acanthopanax root in water at a temperature of 30-60 C for 2-4 hours,
- placing borax and oyster shells in alcohol at a temperature of 60-70 C for 24-48
 - 5 hours, and repeating the cycle three times, alcohol covering said borax and oyster shells,
 - decocting ginseng and notoginseng root in water for 40 minutes, and repeating the cycle three times, water covering the top of said ginseng and notoginseng root by about 1 centimetre;
 - 10 • decocting the cut rhubarb pieces in water for a session of 15 minutes, following by two sessions of 20 minutes, water covering the top of said cut rhubarb pieces by about 1 centimetre;
 - decocting soaked cut herbs selected from the following group: gentian root, Chinese lobelia, unripe bitter orange, white peony, ginger, unsalted fermented
 - 15 soybean, gardenia flower, scutellaria root, houttunzia, bupleurum root, liquorice, spiny jujube kernel, peanut leaf, and manyprickle acanthopanax root together in water for 30 minutes, and repeating the cycle three times, water covering the top of said herbal pieces by about 1 centimetre;
 - combining, distilling and evaporating extracted liquids to produce a dry powder,
 - 20 • adding an effective amount of dried gizzard lining to said dry powder.

14. A method of preparing a medicinal composition for treating drug addiction and insomnia including the steps of :

- 25 • soaking effective amounts of components selected from the following group: gizzard lining, ginseng, notoginseng, rhubarb, gentian root, Chinese lobelia, unripe bitter orange, white peony, ginger, unsalted fermented soybean, gardenia flower, scutellari root, houttunzia, bupleurum root, licorice, spiny jujube kernel, peanut leaf, and manyprickle acanthopanax root in water at a temperature of 30-60 C for
- 30 2-4 hours;

- placing borax and oyster shells in alcohol at a temperature of 60-70 C for 24-48 hours, and repeating the cycle three times, alcohol covering said borax and oyster shells,
 - decocting ginseng and notoginseng root in water for 40 minutes, and repeating the cycle three times, water covering the top of said ginseng and notoginseng root by about 1 centimetre;
 - decocting the cut rhubabr pieces in water for a session of 15 minutes, following by two sessions of 20 minutes, water covering the top of said cut rhubarb pieces by about 1 centimetre;
 - decocting components selected from the following group: gizzard lining, gentian root, Chinese lobelia, unripe bitter orange, white peony, ginger, unsalted fermented soybean, gardenia flower, scutellari root, houttunzia, bupleurum root, liquorice, spiny jujube kernel, peanut leaf, and manyprickle acanthopanax root together in water for 30 minutes, and repeating the cycle three times, water covering the top of said herbal pieces and said gizzard lining by about 1 centimetre;
 - combining, distilling and evaporating extracted liquids to produce a dry powder.
15. A method according to claim 13 or 14 further including placing said powder into a capsule.
16. A method according to claim 15 wherein said capsule contains 0.5 g of said powder.
17. A method according to claim 13 further including the steps of disinfecting Chicken's gallbladder in ethanol, pressing a liquid extract therefrom, and adding said liquid extract to said powder to produce a paste.
18. A method according to claim 17 further including placing said paste into a capsule.

19. A method according to claim 18 wherein said capsule contains 0.5 g of said paste.
20. A method according to claim 14 further including the step of disinfecting
Chicken's gallbladder in ethanol, pressing a liquid extract therefrom, and adding said
5 liquid extract to the liquids extracted from herbal pieces, borax, oyster shells and
gizzard lining prior to the step of distilling and evaporating extracted liquids to
produce a dry powder.
21. A method according to claim 20 further including placing said powder into a
10 capsule.
22. A method according to claim 21 wherein said capsule contains 0.5 g of said
powder.
- 15 23. A medicament for the treatment of drug addiction and insomnia, the medicament
including an effective amount of a composition according to any one of claims 1 to 8.
24. A method for treating drug addiction and insomnia in a patient including
administering to said patient an effective amount of a composition according to any
20 one of claims 1 to 8.
25. A method of treatment for drug addiction as claimed in claim 24, wherein the
herbal composition is administered to the patient orally in three equivalent dosages
which are one third of the amount of a total daily dosage, each dosage being
25 administered in succession in approximately even intervals of about 8 hours each
throughout a day, each dosage being 4-5 capsules.
26. A method of treatment for insomnia as claimed in claim 24, wherein the herbal
composition is administered orally in two equivalent dosages, the first dosage being
30 administered 4 hours prior to a normal sleeping period, the second dosage being
administered approximately 0.5 hour prior to said normal sleeping period, each dosage
being 2 capsules.

27. Use of a composition according to any one of claims 1 to 8 for the manufacture of a medicament for treatment of drug addiction and insomnia.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU02/00649

A. CLASSIFICATION OF SUBJECT MATTERInt. Cl. ⁷: A61K 35/78, 33/22; A61P 25/36, 25/20, 43/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

REFER ELECTRONIC DATABASE CONSULTED BELOW

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

DWPI, CAPLUS, MEDLINE: Keywords: Borax, Borate, Radix Ginseng, Radix Gentianae and similar terms.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Derwent WPAT Abstract Accession No. 97-245837, CN 1100320A (WANG S) 22 March 1995 abstract	1-27
A	Derwent WPAT Abstract Accession No. 2001-426194, CN 1291497A (LIGG), 18 April 2001 abstract	1-27
A	Derwent WPAT Abstract Accession No. 90-052007, CN 1031327A (MAI YAOHUA), 1 March 1989 abstract	1-27

☒ Further documents are listed in the continuation of Box C☐ See patent family annex

* Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

16 July 2002

Date of mailing of the international search report

23 JUL 2002

Name and mailing address of the ISA/AU

AUSTRALIAN PATENT OFFICE
PO BOX 200, WODEN ACT 2606, AUSTRALIA
E-mail address: pct@ipaustralia.gov.au
Facsimile No. (02) 6285 3929

Authorized officer

S. Chew

Telephone No : (02) 6283 2248

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU02/00649

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Derwent WPAT Abstract Accession No. 94-209200, CN 1076627A (MALL) 29 September 1993	1-27
A	Derwent WPAT Abstract Accession No. 2000-476560, CN 1244387A (WANG G), 16 February 2000 abstract	1-27